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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/623,307 | 03/21/2001 | Naoto Oku | 50026/024001 | 2668 |
| 21559 | 7590 | 03/23/2005 | EXAMINER | |
| CLARK & ELBING LLP 101 FEDERAL STREET BOSTON, MA 02110 | | | EPPS FORD, JANET L | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1635 | |

DATE MAILED: 03/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/623,307

Applicant(s)

OKU ET AL.

Examiner

Janet L. Epps-Ford, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 December 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 53-85 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 53-63 is/are allowed.
- 6) ☒ Claim(s) 64-85 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Arguments

1. As stated in the prior Office Action, claims 51, 52, 57, and 61-63 were rejected under 35 USC 112, 2nd paragraph. Applicant's current amendment to the claims canceling claims 51-52 and amending claims 57 and 61 obviates this rejection.

2. Applicant's arguments with respect to the constructive election by original presentation, and non-election of claims 64-81 set forth in the prior Office Action 9-16-2004, were persuasive. Previously presented claims 64-81 and newly added claims 82-85 will be examined with previously examined claims 53-63. An action on the merits of claims 64-85 is set forth below. As stated in the prior Office Action, claims 53-63 are considered allowable over the prior art searched.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 64-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kahne (US 5,780,444).

Instant claim 64 recites: A composition comprising a polyalkylenimine or a salt thereof, wherein said polyalkylenimine or said salt comprises (i) two or more tetraethylenepentamine or spermine structures, and (ii) two or more hydrophobic groups, wherein said polyalkylenimine has a degree of alkylation of less than or equal to 24.5%. Prior art is applied to the extent that

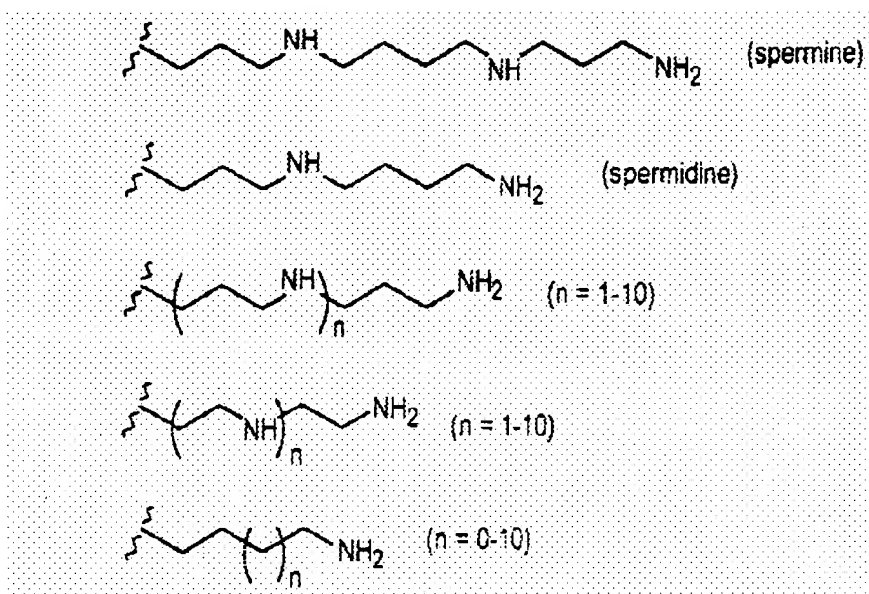
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spermine and tetraethylenepentamine polyalkylenimine structures are considered to have a degree of alkylation of less than or equal to 24.5%, and further that two or more spermine and tetraethylenepentamine polyalkylenimine structures have an average molecule weight of about 600 Da or about 1800 Da. Moreover, it is noted that claims 69-71 do not recite any particular unit of measurement for the molecular weight of the recited polyalkylenimine, however the prior art is applied to the extent that the polyalkylenimine is two or more spermine or tetraethylenepentamine polyalkylenimine structures.

Kahne teaches a method of introducing nucleic acid into cells by transformation. The Kahne invention comprises contacting the cells with nucleic acid in the presence of a compound, which compound comprises a bile acid based molecule and at least one amine containing moiety, preferably a polyamine. In one embodiment of the invention, a lipid, preferably a neutral lipid is present in the contacting step. The transformation medium may also contain cationic lipids (col. 4, lines 33-42).

The method of Kahne comprise contacting a cell with nucleic acid in the presence of a compound of formula I, (see col. 6), this compound has a cholesterol hydrophobic back bone (this portion of Kahne is considered to read on a cholesterol residue, stearyl group, and C₁₆H₃₃ hydrophobic group, see instant claims 83 and 85), wherein said compound is preferably substituted with either spermine, (see compound (F)2 Figure 13), or tetraethylenepentamine (see compound (N)6, Figure 14), at position R₄ in formula I.

Kahne also describe additional examples of polyamines that may be attached to the hydrophobic backbone of formula I, see Figures 3-4 (col. 7, lines 15-17). Figure 3 discloses the following polyamine structures:



The 4th polyamine structure (particularly wherein $n=10$) set forth above encompasses wherein a tetraethylenepentamine is linked in a linear manner.

At Table 2 of Kahne it is disclosed that a 1:1 (w:w) composition of DOPE (dioleyl phosphatidylethanolamine): deoxycholate-spermine conjugate and a 3:1 (w:w) composition of deoxycholate-spermine conjugate: DOPE was useful to efficiently transfect cells with DNA (this portion of Kahne addresses claims 74-77).

Kahne does not explicitly disclose compositions comprising two or more tetraethylenepentamine or spermine structures, and two or more hydrophobic groups, wherein said polyalkylenimine has a degree of alkylation of less than or equal to 24.5%. However, absent evidence to the contrary, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine two or more compounds of Kahne, wherein said compounds are polyamines linked to a cholesterol backbone, and said compounds are useful to deliver nucleic acids to cells, to form a combination with the expectation that said combination would have the same properties as the individual components, namely for delivering nucleic

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acids to cells. See MPEP § 2144.06, "[I]t is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose."

Kahne does not specifically teach polyamines comprising two to five molecules of spermine linked in a linear manner. However, absent evidence to the contrary one of ordinary skill in the art at the time of the instant invention would have been motivated to modify the teachings of Kahne to comprise these structures since the polyamine structures set forth in Figure 3, clearly suggest that spermine is generally useful in the claimed compounds, and linear polyamine structures comprising wherein $n=1-10$, and further comprising wherein there are 2, 3, or 4 carbon atoms separating an amine moiety are useful in the compounds of the Kahne invention.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 69-71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 69 recites "wherein the molecular weight of said polyalkylenimine or said salt is less than or equal to 1,000,000." Claim 70 recites "wherein the molecular weight of said polyalkylenimine or said salt is less than or equal to 500,000." Claim 71 recites, "wherein the molecular weight of said polyalkylenimine or said salt is 500 to 100,000." The metes and bounds of the molecular weight recited in the instant claims is vague and indefinite since there is

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no unit of measurement to accompany the recited numerical values assigned for the molecular weight.


7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 571-272-0757. The examiner can normally be reached on Monday-Saturday, Flex Schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Epps-Ford, Ph.D.
Patent Examiner
Art Unit 1635

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